AMENDMENTS TO THE SPECIFICATION:

Please delete the paragraph on page 6, lines 3-4 and replace it with the following paragraph:

In one embodiment, said fragment is a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**.

Please delete the paragraph on page 6, line 34 to page 7, line 3 and replace it with the following paragraph:

In further embodiments of said process the fragment is a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**, or a fragment comprising the amino acid sequence from about amino acid No. 952 to about amino acid No. 986 of SEQ ID No. 1, or a fragment comprising the amino acid sequence from about amino acid no. 140 to about amino acid no. 337 of SEQ ID no. 1.

Please delete the paragraph on page 7, line 34 to page 8, line 6 and replace it with the following paragraph:

The fragment in said process may be a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the spliced domain. In preferred embodiments said fragment is a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**, or a fragment comprising the amino acid sequence from about amino acid No. 952 to about amino

acid No. 986 of SEQ ID No. 1, or a fragment comprising the amino acid sequence from about amino acid No. 140 to about amino acid no. 337 of SEQ ID No. 1.

Please delete the paragraph on page 8, lines 17-37 and replace it with the following paragraph:

In a still further embodiment this process is a process for detecting the presence of an integrin subunit α10, or a homologue or fragment of said integrin subunit having similar biological activity, on cells, whereby a polynucleotide or oligonucleotide chosen from the group comprising a polynucleotide or oligonucleotide chosen form the nucleotide sequence shown in SEQ ID No. 1 is used as a marker under hybridization conditions wherein said polynucleotide or oligonucleotide fails to hybridise to a DNA or RNA encoding an integrin subunit α1. Said cells may be chosen from the group comprising chondrocytes, smooth muscle cells, endothelial cells, osteoblasts and fibroblasts. Said integrin fragment may be a peptide chosen form the group comprising peptides of the cytoplasmic domain, the I-domain and the spliced domain, such as a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**, or a fragment comprising the amino acid from about amino acid no. 952 to about amino acid no. 986 of SEQ ID No. 1, or a fragment comprising the amino acid sequence from about amino acid No. 140 to about amino acid no. 337 of SEQ ID No. 1.

Please delete the paragraph on page 9, lines 11-37 and replace it with the following paragraph:

The invention also relates to a process for determining the differentiation-state of cells during development, in pathological conditions, in tissue regeneration and in therapeutic and physiological reparation of cartilage, whereby a polynucleotide or oligonucleotide is used as a marker under hybridization conditions wherein said polynucleotide or oligonucleotide is a polynucleotide or ologonucleotide coding for a peptide plasmic domain, the I-domain and the spliced domain, such as a polynucleotide or oligonucleotide coding for a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**, or comprising the amino acid sequence from about amino acid No. 952 to about amino acid no. 986 of SEQ ID No. 1, or the amino acid sequence form about amino acid No. 140 to about amino acid No. 337 of SEQ ID No. 1. Said pathological conditions may be any pathological conditions involving the integrin subunit cancer, or atheroclerosis or inflammation. Said cells may be chosen from the group comprising chondrocytes, smooth nuscle cells, endothelial cells, osteoblasts and fibroblasts.

Please delete the paragraph on page 12, lines 30-31 and replace it with the following paragraph:

Fig. 2. Amino acid sequences of peptides from the bovine α10 integrin subunit **(SEQ ID NOS: 26-31, respectively, in order of appearance)**.

Please delete the paragraph on page 13, lines 8-9 and replace it with the following paragraph:

Fig. 6. Nucleotide sequence **(SEQ ID NO: 1)** and deduced amino acid sequence **(SEQ ID NO: 4)** of the human α10 integrin subunit.

Please delete the paragraph on page 13, lines 29-30 and replace it with the following paragraph:

Fig 15. Partial genomic nucleotide sequence **(SEQ ID NO: 32)** of the human integrin subunit α10 **(Top protein sequence disclosed as SEQ ID NOS: 33-127; middle protein sequence disclosed as SEQ ID NOS: 128-206; bottom protein sequence disclosed as SEQ ID NOS: 207-299)**.

Please delete the paragraph on page 14, line 34 to page 15, line 22 and replace it with the following paragraph:

The deduced amino acid sequence of α10 was found to share the general structure of the integrin α-subunits described in previously published reports (6-21). The large extracellular N-terminal part of α10 contains a seven-fold repeated sequence which was recently predicted to fold into a β-propeller domain (32). The integrin subunit α10 contains three putative divalent cation-binding sites (DxD/NxD/NxxxD) (53), a single spanning transmembrane domain and a short cytoplasmic domain. In contrast to most α-integrin subunits the cytoplasmic domain of α10 does not contain the conserved sequence KxGff (R/K) R **(SEQ ID NO: 22)**. The predicted amino acid sequence in α10 is KLGFFAH **(SEQ ID NO: 8)**. Several reports indicate that the integrin cytoplasmic domains are crucial in signal transduction (54) and that membrane-proximal regions of both α- and β-integrin

cytoplasmic domains are involved in modulating conformation and affinity state of integrins (55-57). It is suggested that the GFFKR **(SEQ ID NO: 23)** motif in α-chains are important for association of integrin subunits and for transport of the inegrin to the plasma membrane (58). The KxGFFKR **(SEQ ID NO: 24)** domain has been shown to interact with the intracellular protein calreticulin (59) and interstingly, calreticulin-null embryonic stem cells are deficient in integrin-mediated cell adhesion (60). It is therefore possible that the sequence KLGFFAH **(SEQ ID NO: 8)** in α10 have a key function in regulating the affinity between α10β1 and matrix proteins.

Please delete the paragraph on page 18, line 33 to page 19, line 14 and replace it with the following paragraph:

The degenerate primers GAY AAY ACI GCI CAR AC **(SEQ ID NO: 9)** (DNTAQT, **SEQ ID NO: 10**, forward) and TIA TIS WRT GRT GIG GYT **(SEQ ID NO: 11)** (EPHHSI, **SEQ ID NO: 12**, reverse) were used in PCR (Camper et al, JBC, 273, 20383-20389 (1998) to amplify the nucleotide sequence corresponding to the bovine peptide 1 (Figure 2). A 900 bp PCR-fragment was then amplicfied from bovine cDNA using an internal specific primer TCA GCC TAC ATT CAT TAT **(SEQ ID NO: 13)** (SAYIQY, **SEQ ID NO: 14**, forward) corresponding to the cloned nucleotide sequence of peptide 1 together with the generate primer ICK RTC CCA RTG ICC IGG **(SEQ ID NO: 15)** (PGHWDP, **SEQ ID NO: 16**, reverse) corresponding to the bovine peptide 2 (Figure2). Mixted bases were used in positions that were twofold degenerate and inosines were used In positions that are three- or fourfold

degenerate. mRNA isolation and cDNA synthesis was done as earlier described (Camper et al, JBC, 273, 20383-20389 (1998)).

Please delete the paragraph on page 19, line 28 to page 20, line 8 and replace it with the following paragraph:

The cloned 900bp PCR-fragment, corresponding to bovine α10-integrin, was digoxigenin-labelled according to the DIG DNA labeling kit (Boehringer Mannheim) and used as a probe for screening of a human articular chondrocyte λZapII cDNA library (provided by Michael Bayliss, The Royal Veterinary Basic Sciences, London, UK)(52). Positive clones containing the pBluescript SK+ plasmid with the cDNA insert were rescued from the ZAP vector by *in vivo* excision as described in the ZAP-cDNA® synthesis kit (Stratagene). Selected plasmids were purified and sequenced as described earlier (Camper et al, JBC, 273, 20383-20389 (1998)) using T3, T7 and internal specific primers. To obtain cDNA that encoded the 5' end of α10 we designed the primer AAC TCG TCT TCC AGT GCC ATT CGT GGG (**SEQ ID NO: 17,** reverse; residue 1254-1280 in α10 cDNA) and used it for rapid amplification of the cDNA 5' end (RACE) as described in the Marathon™ cDNA Amplification kit (Clontech INC., Palo Alto, CA).

Please delete the paragraph on page 6, lines 3-4 and replace it with the following paragraph:

In one embodiment, said fragment is a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**.

Please delete the paragraph on page 6, line 34 to page 7, line 3 and replace it with the following paragraph:

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Please delete the paragraph on page 9, lines 11-37 and replace it with the following paragraph:

The invention also relates to a process for determining the differentiation-state of cells during development, in pathological conditions, in tissue regeneration and in therapeutic and physiological reparation of cartilage, whereby a polynucleotide or oligonucleotide is used as a marker under hybridization conditions wherein said polynucleotide or oligonucleotide is a polynucleotide or ologonucleotide coding for a peptide plasmic domain, the I-domain and the spliced domain, such as a

polynucleotide or oligonucleotide coding for a peptide comprising the amino acid sequence KLGFFAHKKIPEEEKREEKLEQ **(SEQ ID NO: 7)**, or comprising the amino acid sequence from about amino acid No. 952 to about amino acid no. 986 of SEQ ID No. 1, or the amino acid sequence form about amino acid No. 140 to about amino acid No. 337 of SEQ ID No. 1. Said pathological conditions may be any pathological conditions involving the integrin subunit cancer, or atheroclerosis or inflammation. Said cells may be chosen from the group comprising chondrocytes, smooth nuscle cells, endothelial cells, osteoblasts and fibroblasts.

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Fig. 2. Amino acid sequences of peptides from the bovine α10 integrin subunit **(SEQ ID NOS: 26-31, respectively, in order of appearance)**.

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Fig. 6. Nucleotide sequence **(SEQ ID NO: 1)** and deduced amino acid sequence **(SEQ ID NO: 4)** of the human α10 integrin subunit.

Please delete the paragraph on page 13, lines 29-30 and replace it with the following paragraph:

Fig 15. Partial genomic nucleotide sequence **(SEQ ID NO: 32)** of the human integrin subunit α10 **(Top protein sequence disclosed as SEQ ID NOS: 33-127;**

middle protein sequence disclosed as SEQ ID NOS: 128-206; bottom protein sequence disclosed as SEQ ID NOS: 207-299).

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The deduced amino acid sequence of α10 was found to share the general structure of the integrin α-subunits described in previously published reports (6-21). The large extracellular N-terminal part of α10 contains a seven-fold repeated sequence which was recently predicted to fold into a β-propeller domain (32). The integrin subunit α10 contains three putative divalent cation-binding sites (DxD/NxD/NxxxD) (53), a single spanning transmembrane domain and a short cytoplasmic domain. In contrast to most α-integrin subunits the cytoplasmic domain of α10 does not contain the conserved sequence KxGff (R/K) R **(SEQ ID NO: 22)**. The predicted amino acid sequence in α10 is KLGFFAH **(SEQ ID NO: 8)**. Several reports indicate that the integrin cytoplasmic domains are crucial in signal transduction (54) and that membrane-proximal regions of both α- and β-integrin cytoplasmic domains are involved in modulating conformation and affinity state of integrins (55-57). It is suggested that the GFFKR **(SEQ ID NO: 23)** motif in α-chains are important for association of integrin subunits and for transport of the inegrin to the plasma membrane (58). The KxGFFKR **(SEQ ID NO: 24)** domain has been shown to interact with the intracellular protein calreticulin (59) and interstingly, calreticulin-null embryonic stem cells are deficient in integrin-mediated cell adhesion (60). It is therefore possible that the sequence KLGFFAH **(SEQ ID NO: 8)** in α10 have a key function in regulating the affinity between α10β1 and matrix proteins.

Please delete the paragraph on page 18, line 33 to page 19, line 14 and replace it with the following paragraph:

The degenerate primers GAY AAY ACI GCI CAR AC **(SEQ ID NO: 9)** (DNTAQT, **SEQ ID NO: 10**, forward) and TIA TIS WRT GRT GIG GYT **(SEQ ID NO: 11)** (EPHHSI, **SEQ ID NO: 12**, reverse) were used in PCR (Camper et al, JBC, 273, 20383-20389 (1998) to amplify the nucleotide sequence corresponding to the bovine peptide 1 (Figure 2). A 900 bp PCR-fragment was then amplicfied from bovine cDNA using an internal specific primer TCA GCC TAC ATT CAT TAT **(SEQ ID NO: 13)** (SAYIQY, **SEQ ID NO: 14**, forward) corresponding to the cloned nucleotide sequence of peptide 1 together with the generate primer ICK RTC CCA RTG ICC IGG **(SEQ ID NO: 15)** (PGHWDP, **SEQ ID NO: 16**, reverse) corresponding to the bovine peptide 2 (Figure2). Mixted bases were used in positions that were twofold degenerate and inosines were used In positions that are three- or fourfold degenerate. mRNA isolation and cDNA synthesis was done as earlier described (Camper et al, JBC, 273, 20383-20389 (1998)).

Please delete the paragraph on page 19, line 28 to page 20, line 8 and replace it with the following paragraph:

The cloned 900bp PCR-fragment, corresponding to bovine α10-integrin, was digoxigenin-labelled according to the DIG DNA labeling kit (Boehringer Mannheim) and used as a probe for screening of a human articular chondrocyte λZapII cDNA library (provided by Michael Bayliss, The Royal Veterinary Basic Sciences, London,

UK)(52). Positive clones containing the pBluescript SK+ plasmid with the cDNA insert were rescued from the ZAP vector by *in vivo* excision as described in the ZAP-cDNA® synthesis kit (Stratagene). Selected plasmids were purified and sequenced as described earlier (Camper et al, JBC, 273, 20383-20389 (1998)) using T3, T7 and internal specific primers. To obtain cDNA that encoded the 5' end of α10 we designed the primer AAC TCG TCT TCC AGT GCC ATT CGT GGG (**SEQ ID NO: 17,** reverse; residue 1254-1280 in α10 cDNA) and used it for rapid amplification of the cDNA 5' end (RACE) as described in the Marathon™ cDNA Amplification kit (Clontech INC., Palo Alto, CA).

Please delete the paragraph on page 22, lines 4-10 and replace it with the following paragraph:

A peptide corresponding to part of the α10 cytoplasmic domain, Ckkipeeekreekle (**SEQ ID NO: 25,** see figure 6) was synthesized and conjugated to keyhole limpet hemocyanin (KLH). Rabbits were immunized with the peptide-KLH conjugate to generate antiserum against the integrin subunit α10. Antibodies recognizing α10 were affinity purified on an peptide-coupled column (Innovagen AB).

Please delete the paragraph on page 29, line 27 to page 30, line 9 and replace it with the following paragraph:

A plasmid for intracellular expression in E. coli of the alternatively spliced region (amino acid pos. 952-986, SEQ ID 1) was constructed as described. The alternatively spliced region were back-translated using the E. coli high frequency

codon table, creating a cDNA sequence of 96% identity with the origin sequence (SEQ. ID 1 nucleotide pos 2940-3044). Using sequence overlap extension (Horton et al., Biotechniques 8:528, 1990) primer α10pfor (tab. I) and α10 prev (tab. I) was used to generate a double stranded fragment encoding the α10 amino acid sequence. This fragment was used as a PCR template with primers α10pfor2 (tab. I) and α10prev2 (tab. I) in order to generate restriction enzyme site for sub-cloning in a pET vector containing the Z-domain of staphylococcal protein A, creating a fusion of the α10 spliced region with the amino terminal of the Z-domain with trombin cleavage site residing in-between. The fragment generated in the second PCR reaction is shown (SEQ ID No. 3**; amino acid sequence disclosed as SEQ ID NO: 6**) also indicating the unique restriction enzymes used for sub-cloning in the expression vector.

Please delete the Table 1 header on page 30 and replace it with the following header:

Table I **(SEQ ID NOS: 18-21, respectively, in order of appearance)**

Please delete the paragraph on page 22, lines 4-10 and replace it with the following paragraph:

A peptide corresponding to part of the α10 cytoplasmic domain, Ckkipeeekreekle (**SEQ ID NO: 25,** see figure 6) was synthesized and conjugated to keyhole limpet hemocyanin (KLH). Rabbits were immunized with the peptide-KLH conjugate to generate antiserum against the integrin subunit α10. Antibodies recognizing α10 were affinity purified on an peptide-coupled column (Innovagen AB).

Please delete the paragraph on page 29, line 27 to page 30, line 9 and replace it with the following paragraph:

A plasmid for intracellular expression in E. coli of the alternatively spliced region (amino acid pos. 952-986, SEQ ID 1) was constructed as described. The alternatively spliced region were back-translated using the E. coli high frequency codon table, creating a cDNA sequence of 96% identity with the origin sequence (SEQ. ID 1 nucleotide pos 2940-3044). Using sequence overlap extension (Horton et al., Biotechniques 8:528, 1990) primer α10pfor (tab. I) and α10 prev (tab. I) was used to generate a double stranded fragment encoding the α10 amino acid sequence. This fragment was used as a PCR template with primers α10pfor2 (tab. I) and α10prev2 (tab. I) in order to generate restriction enzyme site for sub-cloning in a pET vector containing the Z-domain of staphylococcal protein A, creating a fusion of the α10 spliced region with the amino terminal of the Z-domain with trombin cleavage site residing in-between. The fragment generated in the second PCR reaction is shown (SEQ ID No. 3**; amino acid sequence disclosed as SEQ ID NO: 6**) also indicating the unique restriction enzymes used for sub-cloning in the expression vector.

Please delete the Table 1 header on page 30 and replace it with the following header:

Table I **(SEQ ID NOS: 18-21, respectively, in order of appearance)**